VAXNEUVANCE- pneumococcal 15-valent conjugate vaccine crm197 protein adsorbed injection, suspension
Merck Sharp & Dohme Corp.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VAXNEUVANCE safely and effectively. See full prescribing information for VAXNEUVANCE.

VAXNEUVANCE™ (Pneumococcal 15-valent Conjugate Vaccine)
Suspension for Intramuscular Injection
Initial U.S. Approval: 2021

INDICATIONS AND USAGE

VAXNEUVANCE™ is a vaccine indicated for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in adults 18 years of age and older. (1)

DOSAGE AND ADMINISTRATION

For intramuscular use only.
Administer a single 0.5 mL dose. (2.1)

DOSAGE FORMS AND STRENGTHS

Suspension for injection (0.5 mL dose), supplied as a single-dose prefilled syringe. (3)

CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) to any component of VAXNEUVANCE or to diphtheria toxoid. (4)

ADVERSE REACTIONS

The most commonly reported solicited adverse reactions:

- in individuals 18 through 49 years of age were: injection-site pain (75.8%), fatigue (34.3%), myalgia (28.8%), headache (26.5%), injection-site swelling (21.7%), injection-site erythema (15.1%) and arthralgia (12.7%). (6.1)
- in individuals 50 years of age and older were: injection-site pain (66.8%), myalgia (26.9%), fatigue (21.5%), headache (18.9%), injection-site swelling (15.4%), injection-site erythema (10.9%) and arthralgia (7.7%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.
See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 7/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VAXNEUVANCE™ is indicated for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in adults 18 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular use only.

2.1 Dosage

Administer a single 0.5 mL dose.

2.2 Administration

Hold the prefilled syringe horizontally and shake vigorously immediately prior to use to obtain an opalescent suspension in the prefilled syringe. Do not use the vaccine if it cannot be resuspended. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use if particulate matter or discoloration is observed.

3 DOSAGE FORMS AND STRENGTHS

VAXNEUVANCE is a suspension for intramuscular injection supplied in a 0.5 mL single-dose prefilled syringe.

4 CONTRAINDICATIONS

Do not administer VAXNEUVANCE to individuals with a severe allergic reaction (e.g., anaphylaxis) to any component of VAXNEUVANCE or to diphtheria toxoid. *[See Description (11).]*

5 WARNINGS AND PRECAUTIONS

5.1 Altered Immunocompetence

Some individuals with altered immunocompetence, including those receiving immunosuppressive therapy, may have a reduced immune response to VAXNEUVANCE. *[See Drug Interactions (7.1) and Use in Specific Populations (8.6).]*

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The most commonly reported solicited adverse reactions in individuals 18 through 49 years of age were: injection-site pain (75.8%), fatigue (34.3%), myalgia (28.8%), headache (26.5%), injection-site swelling (21.7%), injection-site erythema (15.1%) and arthralgia (12.7%).

The most commonly reported solicited adverse reactions in individuals 50 years of age and older were: injection-site pain (66.8%), myalgia (26.9%), fatigue (21.5%), headache (18.9%), injection-site swelling (15.4%), injection-site erythema (10.9%) and arthralgia (7.7%).

Safety Assessment in Clinical Studies

The safety of VAXNEUVANCE was assessed in 7 randomized, double-blind clinical studies conducted in the Americas, Europe and Asia Pacific, in which 5,630 adults 18 years of age and older received VAXNEUVANCE and 1,808 adults received Prevnar 13 [Pneumococcal 13-valent Conjugate Vaccine (Diphtheria CRM_{197} Protein)]. In Studies 1-3 (NCT03950622, NCT03950856, and NCT03480763), a total of 3,032 adults 50 years of age and older with no history of pneumococcal vaccination received VAXNEUVANCE and 1,154 participants received Prevnar 13. In Study 4 (NCT03547167), adults 18 through 49 years of age with no history of pneumococcal vaccination, including individuals with increased risk of developing pneumococcal disease, received VAXNEUVANCE (N=1,134) or Prevnar 13 (N=378), followed by PNEUMOVAX 23 six months later. In Study 5 (NCT02573181), adults 65 years of age and older previously vaccinated with PNEUMOVAX 23 (at least 1 year prior to study entry) received VAXNEUVANCE (N=127) or Prevnar 13 (N=126). In Study 6 (NCT03615482), adults 50 years of age and older received VAXNEUVANCE concomitantly with a seasonal inactivated quadrivalent

influenza vaccine (Fluarix Quadrivalent; QIV) (Group 1, N=600) or nonconcomitantly 30 days after QIV (Group 2, N=585). In this study population, 20.9% of individuals had a history of prior vaccination with PNEUMOVAX 23. In Study 7 (NCT03480802), HIV-infected adults 18 years of age and older received VAXNEUVANCE (N=152) or Prevnar 13 (N=150), followed by PNEUMOVAX 23 two months later.

The clinical studies included adults with stable underlying medical conditions (e.g., diabetes mellitus, renal disorders, chronic heart disease, chronic liver disease, chronic lung disease including asthma) and/or behavioral risk factors (e.g., smoking, increased alcohol use) that are known to increase the risk of pneumococcal disease. Overall, the mean age of the participants was 58 years and 54.6% were female. The racial distribution was as follows: 72.3% were White, 9.9% were Asian, 8.1% were American Indian or Alaska Native, 7.4% were Black or African American, and 18.1% were of Hispanic or Latino ethnicity.

In all studies, safety was monitored using a Vaccination Report Card (VRC) for up to 14 days postvaccination. Study investigators reviewed the VRC with the participants 15 days postvaccination to ensure consistency with protocol definitions. The analyses presented in Tables 1-3 below reflect the information based on the final assessment by the study investigators. Oral body temperature and injection-site adverse reactions were solicited on Day 1 through Day 5 postvaccination. Systemic adverse reactions were solicited on Day 1 through Day 14 postvaccination. Unsolicited adverse events were reported on Day 1 through Day 14 postvaccination.

The duration of the safety follow-up period for serious adverse events postvaccination with VAXNEUVANCE was 1 month in Study 5; 2 months in Study 7; 6 months in Studies 1, 2, 4 and 6; and 12 months in Study 3.

Solicited Adverse Reactions

The percentage of participants with solicited adverse reactions that occurred within 5 or 14 days following administration of VAXNEUVANCE or Prevnar 13 in 3 studies are shown in Tables 1-3. The majority of solicited adverse reactions lasted ≤3 days.

Table 1: Percentage of Participants with Solicited Local and Systemic Adverse Reactions in Pneumococcal Vaccine-Naïve Adults 50 Years of Age and Older (Study 2)*

	VAXNEUVANCE (%) N=2,103	**Prevnar 13 (%) N=230**
Local Reactions†		
Pain		
Any	66.8	52.2
Grade 3‡	0.9	0.0
Erythema		
Any	10.9	9.6
>10 cm	0.6	0.4
Swelling		
Any	15.4	14.3
>10 cm	0.2	0.0
Systemic Reactions§		

Fatigue		
Any	21.5	22.2
Grade 3‡	0.7	0.9
Headache		
Any	18.9	18.7
Grade 3‡	0.8	0.0
Myalgia		
Any	26.9	21.7
Grade 3‡	0.4	0.0
Arthralgia		
Any	7.7	5.7
Grade 3‡	0.2	0.0
Fever† ¶		
≥38.0°C and <38.5°C	0.6	0.4
≥38.5°C and <39.0°C	0.1	0.0
≥39.0°C	0.0	0.0

N=Number of participants vaccinated

* Study 2 (NCT03950856) was a randomized (9:1), double-blind, active comparator-controlled, lot to lot consistency study. Safety was monitored using a Vaccination Report Card (VRC) for up to 14 days postvaccination. The table represents the final assessment by the study investigators upon review of the VRC 15 days postvaccination, to ensure consistency with protocol definitions.
† Solicited on Day 1 through Day 5 postvaccination
‡ Any use of narcotic pain reliever or prevents daily activity
§ Solicited on Day 1 through Day 14 postvaccination
¶ Percentages are based on the number of participants with temperature data

Table 2: Percentage of Participants with Solicited Local and Systemic Adverse Reactions in Pneumococcal Vaccine-Naïve Adults 18 to 49 Years of Age With or Without Risk Factors for Pneumococcal Disease (Study 4)*

	VAXNEUVANCE (%) N=1,134	**Prevnar 13 (%) N=378**
Local Reactions†		
Pain		
Any	75.8	68.8
Grade 3‡	1.1	1.6
Erythema		
Any	15.1	14.0
>10 cm	0.5	0.3
Swelling		
Any	21.7	22.2
>10 cm	0.4	0.5
Systemic Reactions§		
Fatigue		
Any	34.3	36.8
Grade 3‡	1.0	0.8

Headache		
Any	26.5	24.9
Grade 3‡	0.8	0.5
Myalgia		
Any	28.8	26.5
Grade 3‡	0.3	0.5
Arthralgia		
Any	12.7	11.6
Grade 3‡	0.4	0.0
Fever† ¶		
≥38.0°C and <38.5°C	1.0	0.3
≥38.5°C and <39.0°C	0.3	0.0
≥39.0°C	0.2	0.0

N=Number of participants vaccinated

* Study 4 (NCT03547167) was a randomized (3:1), double-blind, descriptive study. Safety was monitored using a Vaccination Report Card (VRC) for up to 14 days postvaccination. The table represents the final assessment by the study investigators upon review of the VRC 15 days postvaccination, to ensure consistency with protocol definitions.

† Solicited on Day 1 through Day 5 postvaccination

‡ Any use of narcotic pain reliever or prevents daily activity

§ Solicited on Day 1 through Day 14 postvaccination

¶ Percentages are based on the number of participants with temperature data

Table 3: Percentage of Participants with Solicited Local and Systemic Adverse Reactions in Adults 65 Years of Age and Older with Previous Pneumococcal Vaccination (Study 5)*

	VAXNEUVANCE (%) N=127	**Prevnar 13 (%) N=126**
Local Reactions†		
Pain		
Any	55.1	44.4
Grade 3‡	0.8	0.0
Erythema		
Any	7.9	7.1
>10 cm	0.8	0.0
Swelling		
Any	14.2	6.3
>10 cm	0.0	0.0
Systemic Reactions§		
Fatigue		
Any	18.1	19.0
Grade 3‡	0.0	0.0
Headache		
Any	13.4	15.9
Grade 3‡	0.0	0.0
Myalgia		

Any	15.7	11.1
Grade 3‡	0.8	0.0
Arthralgia		
Any	5.5	8.7
Grade 3‡	0.0	0.0
Fever† ¶		
≥38.0°C and <38.5°C	1.6	0.0
≥38.5°C and <39.0°C	0.0	0.0
≥39.0°C	0.0	0.0

N=Number of participants vaccinated

* Study 5 (NCT02573181) was a randomized, double-blind, descriptive study. Safety was monitored using a Vaccination Report Card (VRC) for up to 14 days postvaccination. The table represents the final assessment by the study investigators upon review of the VRC 15 days postvaccination, to ensure consistency with protocol definitions.
† Solicited on Day 1 through Day 5 postvaccination
‡ Any use of narcotic pain reliever or prevents daily activity
§ Solicited on Day 1 through Day 14 postvaccination
¶ Percentages are based on the number of participants with temperature data

Unsolicited Adverse Reactions

Across all studies, injection-site pruritus was reported to occur in up to 2.8% of adults vaccinated with VAXNEUVANCE.

Serious Adverse Events

Across all studies, among participants 18 years of age and older who received VAXNEUVANCE (excluding those who received QIV concomitantly; N=5,030) or Prevnar 13 (N=1,808), serious adverse events within 30 days postvaccination were reported by 0.4% of VAXNEUVANCE recipients and by 0.7% of Prevnar 13 recipients. In a subset of these studies, among those who received VAXNEUVANCE (N=4,751) and Prevnar 13 (N=1,532), serious adverse events within 6 months postvaccination were reported by 2.5% of VAXNEUVANCE recipients and by 2.4% of Prevnar 13 recipients.

There were no notable patterns or numerical imbalances between vaccination groups for specific categories of serious adverse events that would suggest a causal relationship to VAXNEUVANCE.

Safety with Concomitant Influenza Vaccine Administration

The safety profile was similar when VAXNEUVANCE was administered with or without inactivated quadrivalent influenza vaccine.

7 DRUG INTERACTIONS

7.1 Immunosuppressive Therapies

Immunosuppressive therapies may reduce the immune response to this vaccine *[see Warnings and Precautions (5.1)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

There are no adequate and well-controlled studies of VAXNEUVANCE in pregnant women. Available data on VAXNEUVANCE administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

Developmental toxicity studies have been performed in female rats administered a human dose of VAXNEUVANCE on four occasions; twice prior to mating, once during gestation and once during lactation. These studies revealed no evidence of harm to the fetus due to VAXNEUVANCE *[see Animal Data below]*.

Data

Animal Data

Developmental toxicity studies have been performed in female rats. In these studies, female rats received a human dose of VAXNEUVANCE by intramuscular injection on day 28 and day 7 prior to mating, and on gestation day 6 and on lactation day 7. No vaccine related fetal malformations or variations were observed. No adverse effect on pup weight up to post-natal day 21 was noted.

8.2 Lactation

Risk Summary

Human data are not available to assess the impact of VAXNEUVANCE on milk production, its presence in breast milk, or its effects on the breastfed child. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for VAXNEUVANCE and any potential adverse effects on the breastfed child from VAXNEUVANCE or from the underlying maternal condition. For preventive vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

The safety and effectiveness of VAXNEUVANCE in individuals younger than 18 years of age have not been established.

8.5 Geriatric Use

Of the 4,389 individuals aged 50 years and older who received VAXNEUVANCE, 2,478 (56.5%) were 65 years and older, and 479 (10.9%) were 75 years and older *[see Adverse Reactions (6.1) and Clinical Studies (14.1)].* Overall, there were no clinically meaningful differences in the safety profile or immune responses observed in older individuals (65 to 74 years and 75 years of age and older) when compared to younger individuals.

8.6 Individuals at Increased Risk for Pneumococcal Disease

Adults with HIV Infection

In a double-blind, descriptive study (Study 7), the safety and immunogenicity of VAXNEUVANCE were evaluated in pneumococcal vaccine-naïve HIV-infected adults 18 years of age and older, with CD4+ T-cell count ≥50 cells per microliter and plasma HIV RNA value <50,000 copies/mL. Participants were randomized to receive VAXNEUVANCE (N=152) or Prevnar 13 (N=150), followed by PNEUMOVAX 23 two months later *[see Adverse Reactions (6.1)]*. Anti-pneumococcal opsonophagocytic activity (OPA) geometric mean antibody titers (GMTs) were higher after administration of VAXNEUVANCE, compared to pre-vaccination, for the 15 serotypes contained in VAXNEUVANCE. After sequential administration with PNEUMOVAX 23, OPA GMTs observed at 30 days after PNEUMOVAX 23 vaccination were numerically similar between the two vaccination groups for all 15 serotypes contained in VAXNEUVANCE. The safety profile of VAXNEUVANCE was similar between the two vaccination groups. The effectiveness of VAXNEUVANCE in HIV-infected individuals has not been evaluated.

11 DESCRIPTION

VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine) is a sterile suspension of purified capsular polysaccharides from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F individually conjugated to CRM_{197}. Each pneumococcal capsular polysaccharide is activated via sodium metaperiodate oxidation and then individually conjugated to CRM_{197} carrier protein via reductive amination. CRM_{197} is a non-toxic variant of diphtheria toxin (originating from *Corynebacterium diphtheriae* C7) expressed recombinantly in *Pseudomonas fluorescens*.

Each of the fifteen serotypes is manufactured independently using the same manufacturing steps with slight variations to accommodate for differences in strains, polysaccharides and process stream properties. Each *S. pneumoniae* serotype is grown in media containing yeast extract, dextrose, salts and soy peptone. Each polysaccharide is purified by a series of chemical and physical methods. Then each polysaccharide is chemically activated and conjugated to the carrier protein CRM_{197} to form each glycoconjugate. CRM_{197} is isolated from cultures grown in a glycerol-based, chemically-defined, salt medium and purified by chromatography and ultrafiltration. The final vaccine is prepared by blending the fifteen glycoconjugates with aluminum phosphate adjuvant in a final buffer containing histidine, polysorbate 20 and sodium chloride.

Each 0.5 mL dose contains 2.0 mcg each of *S. pneumoniae* polysaccharide serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4.0 mcg of polysaccharide serotype 6B, 30 mcg of CRM_{197} carrier protein, 1.55 mg L-histidine, 1 mg of polysorbate 20, 4.50 mg sodium chloride, and 125 mcg of aluminum as aluminum phosphate adjuvant. VAXNEUVANCE does not contain any preservatives.

The tip cap and plunger stopper of the prefilled syringe are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Protection against invasive disease is conferred mainly by opsonophagocytic killing of *S.*

pneumoniae. VAXNEUVANCE induces opsonophagocytic activity against the serotypes contained in the vaccine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

VAXNEUVANCE has not been evaluated for carcinogenic or mutagenic potential or for impairment of male fertility in animals. VAXNEUVANCE administered to female rats had no effect on fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

Immune responses elicited by VAXNEUVANCE and Prevnar 13 were measured by a multiplexed opsonophagocytic antibody assay (MOPA) for the 15 pneumococcal serotypes contained in VAXNEUVANCE pre- and post- vaccination.

14.1 Clinical Trials in Pneumococcal Vaccine-Naïve Adults

Study 1

Study 1 assessed serotype-specific opsonophagocytic activity (OPA) responses for each of the 15 serotypes contained in VAXNEUVANCE at 30 days postvaccination in a double-blind, active comparator-controlled study that enrolled pneumococcal vaccine-naïve participants 50 years of age and older. Participants were randomized to receive either VAXNEUVANCE (N=604) or Prevnar 13 (N=601) at sites in USA, Canada, Spain, Taiwan, and Japan. The mean age of participants was 66 years and 57.3% were female. The racial distribution was as follows: 67.7% were White, 25.1% were Asian, 6.1% were Black or African American and 22.0% were of Hispanic or Latino ethnicity.

Table 4 summarizes the OPA geometric mean antibody titers (GMTs) at 30 days postvaccination for the 15 serotypes contained in VAXNEUVANCE. The study demonstrated that VAXNEUVANCE is noninferior to Prevnar 13 for the 13 shared serotypes and induces statistically significantly greater OPA GMTs compared to Prevnar 13 for shared serotype 3 and for the 2 unique serotypes (22F, 33F).

Table 4: Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults 50 Years of Age and Older (Study 1)

Pneumococcal Serotype	VAXNEUVANCE (N = 602)		Prevnar 13 (N = 600)		GMT Ratio* (VAXNEUVANCE/Prevnar 13) (95% CI)*
	n	GMT*	n	GMT*	
Serotype†					
1	598	257	598	321	0.80 (0.66, 0.97)
3‡	598	215	598	133	1.62 (1.40, 1.87)
4	598	1109	598	1633	0.68 (0.57, 0.80)
5	598	445	598	560	0.79 (0.64, 0.98)
6A	596	5371	596	5276	1.02 (0.85, 1.22)
6B	598	3984	598	3179	1.25 (1.04, 1.51)

7F	596	4575	596	5830	0.78 (0.68, 0.90)
9V	598	1809	597	2193	0.83 (0.71, 0.96)
14	598	1976	598	2619	0.75 (0.64, 0.89)
18C	598	2749	598	2552	1.08 (0.91, 1.27)
19A	598	3177	597	3921	0.81 (0.70, 0.94)
19F	598	1688	598	1884	0.90 (0.77, 1.04)
23F	598	2029	598	1723	1.18 (0.96, 1.44)
Additional Serotypes§					
22F	594	2381	585	73	32.52 (25.87, 40.88)
33F	598	8010	597	1114	7.19 (6.13, 8.43)

N=Number of participants randomized and vaccinated; n=Number of participants contributing to the analysis that had at least one pre-dose OPA measurement (VAXNEUVANCE, n=537-597; Prevnar 13, n=545-595) or post-dose OPA measurement (VAXNEUVANCE, n=568-580; Prevnar 13, n=528-574).
CI=confidence interval; cLDA=constrained longitudinal data analysis; GMT=geometric mean titer; OPA=opsonophagocytic activity

* GMTs, GMT ratio, and 95% CI are estimated from a cLDA model.
† Non-inferiority for the 13 shared serotypes was met if the lower bound of the 95% CI for the GMT ratio (VAXNEUVANCE/Prevnar 13) was > 0.5.
‡ Statistically significantly greater OPA GMT for serotype 3 was based on the lower bound of the 95% CI for the estimated GMT ratio (VAXNEUVANCE/Prevnar 13) > 1.2.
§ Statistically significantly greater OPA GMTs for serotypes 22F and 33F was based on the lower bound of the 95% CI for the estimated GMT ratio (VAXNEUVANCE/Prevnar 13) > 2.0.

Study 3

In a double-blind, active comparator-controlled, descriptive study (Study 3), pneumococcal vaccine-naïve adults 50 years of age and older were randomized to receive either VAXNEUVANCE (N=327) or Prevnar 13 (N=325), followed by PNEUMOVAX 23 one year later.

Following vaccination with PNEUMOVAX 23, OPA GMTs were numerically similar between the two vaccination groups for the 15 serotypes in VAXNEUVANCE.

Study 4

In a double-blind, descriptive study (Study 4), adults 18 through 49 years of age, including individuals with increased risk of developing pneumococcal disease, were randomized to receive VAXNEUVANCE (N=1,135) or Prevnar 13 (N=380), followed by PNEUMOVAX 23 six months later *[see Adverse Reactions (6.1)]*. Among those who received VAXNEUVANCE, 620 participants had one risk factor and 228 participants had two or more risk factors for pneumococcal disease.

Table 5 presents OPA GMTs in the overall study population for each of the 15 serotypes 30 days following vaccination with VAXNEUVANCE or Prevnar 13.

Table 5: Serotype-Specific OPA GMTs in Pneumococcal Vaccine-Naïve Adults 18 through 49 Years of Age With or Without Risk

Factors for Pneumococcal Disease (Study 4)

Pneumococcal Serotype	VAXNEUVANCE (N = 1,133)			Prevnar 13 (N = 379)		
	n	Observed GMT	95% CI*	n	Observed GMT	95% CI*
Serotype						
1	1004	267	(242, 295)	337	267	(220, 324)
3	990	198	(184, 214)	336	150	(129, 173)
4	1001	1401	(1294, 1517)	338	2568	(2268, 2908)
5	1003	560	(508, 618)	339	731	(613, 873)
6A	994	12763	(11772, 13838)	333	11313	(9739, 13141)
6B	999	10164	(9486, 10891)	338	6958	(5987, 8086)
7F	1004	5725	(5382, 6090)	338	7583	(6762, 8503)
9V	1000	3353	(3132, 3590)	339	3969	(3541, 4449)
14	1001	5245	(4860, 5660)	339	5863	(5191, 6623)
18C	999	5695	(5314, 6103)	339	3050	(2685, 3465)
19A	1001	5335	(4985, 5710)	339	5884	(5221, 6632)
19F	1003	3253	(3051, 3468)	339	3272	(2949, 3631)
23F	1001	4828	(4443, 5247)	337	3876	(3323, 4521)
Additional Serotypes						
22F	991	3939	(3654, 4246)	317	291	(221, 383)
33F	999	11734	(10917, 12612)	334	2181	(1826, 2606)

N=Number of participants randomized and vaccinated; n=Number of participants contributing to the analysis.
CI=confidence interval; GMT=geometric mean titer;
OPA=opsonophagocytic activity.

* The within-group 95% CIs are obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution.

Following vaccination with PNEUMOVAX 23, the OPA GMTs for the 15 serotypes in VAXNEUVANCE were numerically similar among subjects who had received

VAXNEUVANCE or Prevnar 13 for the first vaccination.

14.2 Concomitant Vaccination

In a double-blind, randomized study (Study 6), adults 50 years of age and older were randomized to receive VAXNEUVANCE concomitantly administered with a seasonal inactivated quadrivalent influenza vaccine (Fluarix Quadrivalent; QIV) (Group 1, N=600) or VAXNEUVANCE 30 days after receiving QIV (Group 2, N=600) *[see Adverse Reactions (6)]*. Pneumococcal vaccine serotype OPA GMTs were evaluated 30 days after VAXNEUVANCE and influenza vaccine strain hemagglutinin inhibition assay (HAI) GMTs were evaluated 30 days after QIV. The noninferiority criteria for the comparisons of GMTs [lower limit of the 2-sided 95% confidence interval (CI) of the GMT ratio (Group 1/Group 2) >0.5] were met for the 15 pneumococcal serotypes in VAXNEUVANCE and for the 4 influenza vaccine strains tested.

16 HOW SUPPLIED/STORAGE AND HANDLING

VAXNEUVANCE is supplied as follows:

Carton of one 0.5 mL single-dose prefilled Luer Lock syringes with tip caps. NDC 0006-4329-02

Carton of ten 0.5 mL single-dose prefilled Luer Lock syringes with tip caps. NDC 0006-4329-03

Store refrigerated at 2°C to 8°C (36°F to 46°F).

Do not freeze. Protect from light.

The tip cap and plunger stopper of the prefilled syringe are not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Discuss the following with the patient:

- Provide the required vaccine information to the patient.
- Inform the patient of the benefits and risks associated with vaccination.
- Inform the patient that vaccination with VAXNEUVANCE may not protect all vaccine recipients.
- Instruct the patient to report any serious adverse reactions to their healthcare provider who in turn should report such events to the vaccine manufacturer or the U.S. Department of Health and Human Services through the Vaccine Adverse Event Reporting System (VAERS), 1-800-822-7967, or report online at www.vaers.hhs.gov.

Manufactured by: Merck Sharp & Dohme Corp., a subsidiary of
MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

U.S. license number 0002

For patent information: www.merck.com/product/patent/home.html

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Patient Information
VAXNEUVANCE™ (pronounced "VAKS-noo-vans")
(Pneumococcal 15-valent Conjugate Vaccine)

Before you get VAXNEUVANCE™, read this information sheet and be sure you understand it. If you have questions or experience any side effects, talk to your healthcare provider. This information does not take the place of talking about VAXNEUVANCE with your healthcare provider. Your healthcare provider will decide if VAXNEUVANCE is right for you.

What is VAXNEUVANCE?

- VAXNEUVANCE is a vaccine for adults 18 years of age and older to help protect against invasive disease caused by 15 types of pneumococcus (pronounced "noo-mo-ca-cus"), a kind of bacteria. Invasive disease includes:
  - an infection in the blood (bacteremia).
  - an infection of the coverings of the brain and spinal cord (meningitis).
- VAXNEUVANCE will not give you disease caused by pneumococcus.
- VAXNEUVANCE might not protect everyone who gets the vaccine.

Who should not get VAXNEUVANCE?

Do not get VAXNEUVANCE if you:

- have or had an allergic reaction to any of the ingredients in VAXNEUVANCE or to diphtheria toxoid. (See the list of ingredients at the end of this information sheet.)

What should I tell my healthcare provider before getting VAXNEUVANCE?

Tell your healthcare provider if you:

- have or had an allergic reaction to any vaccine.
- have a weak immune system (which means your body has a hard time fighting off infections).
- take medicines or treatments that might weaken your immune system (like immunosuppressants or steroids).
- are pregnant or planning to get pregnant.
- are breast-feeding.

How is VAXNEUVANCE given?

VAXNEUVANCE is given as an injection into the muscle (usually in your upper arm).

What are the possible side effects of VAXNEUVANCE?

The most common side effects seen with VAXNEUVANCE are:

- Pain, swelling or redness where you got the injection

- Feeling tired
- Muscle aches
- Headache
- Joint pain

These side effects generally last three days or less.

If you have any side effects that bother you or any other unusual symptoms that develop after you get this injection, tell your healthcare provider. Tell your healthcare provider right away if you have symptoms of an allergic reaction which may include:

- Difficulty breathing
- Swelling of your face, lips, tongue or throat
- Hives
- Rash

There may be side effects that are not listed here. For more information, ask your healthcare provider.

You may also report any side effects to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or directly to Vaccine Adverse Event Reporting System (VAERS). The VAERS toll-free number is 1-800-822-7967 or report online to www.vaers.hhs.gov.

What are the ingredients in VAXNEUVANCE?

Active ingredient: Bacterial sugars from 15 types of pneumococcus each linked to a protein (CRM_{197}). The sugars from these bacteria and the protein are not alive and do not cause disease.
Inactive ingredients: Sodium chloride, L-histidine, polysorbate 20 and aluminum (aluminum phosphate is included to help the vaccine work better).

VAXNEUVANCE does not have any preservatives.

The tip cap and plunger stopper of the prefilled syringe are not made with natural rubber latex.

What if I have other questions?

If you have questions about VAXNEUVANCE, talk to your healthcare provider or call the Merck National Service Center at 1-800-622-4477.

Manufactured by: Merck Sharp & Dohme Corp., a subsidiary of
MERCK & CO., INC., Whitehouse Station, NJ 08889, USA

For patent information: www.merck.com/product/patent/home.html

usppi-v114-i-2107r000

This Patient Information has been approved by the U.S. Food and Drug Administration.

Issued: 07/2021

PRINCIPAL DISPLAY PANEL - 0.5 mL Syringe Carton

NDC 0006-4329-03
10 Single-dose 0.5 mL Syringes

REFRIGERATE

Pneumococcal 15-valent
Conjugate Vaccine
VAXNEUVANCE™

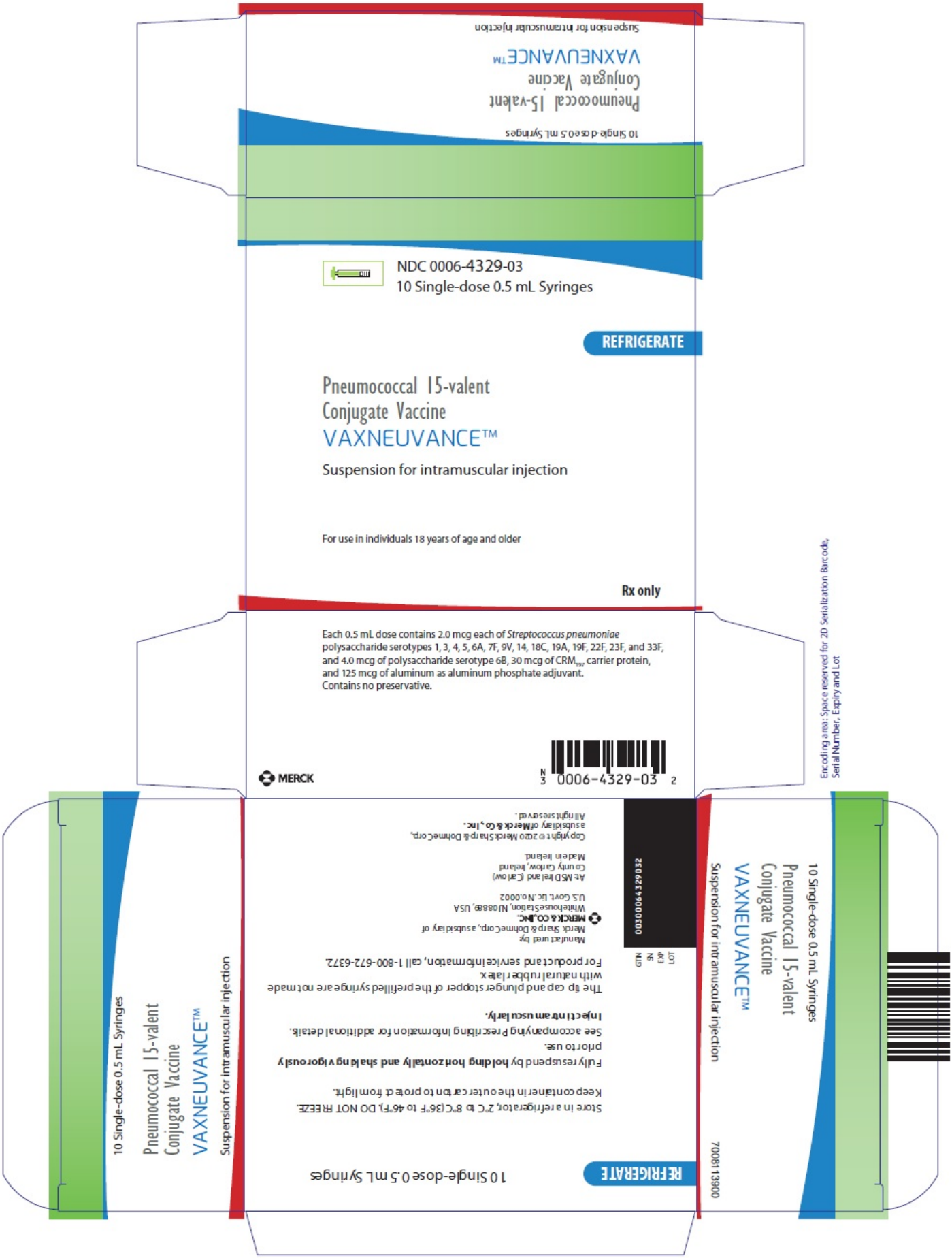
Suspension for intramuscular injection

For use in individuals 18 years of age and older

Rx only

Each 0.5 mL dose contains 2.0 mcg each of *Streptococcus pneumoniae* polysaccharide serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4.0 mcg of polysaccharide serotype 6B, 30 mcg of CRM_{197} carrier protein, and 125 mcg of aluminum as aluminum phosphate adjuvant.
Contains no preservative.

MERCK


Suspension for intramuscular injection
Pneumococcal 15-valent
Conjugate Vaccine
VAXNEUVANCE™
10 Single-dose 0.5 mL Syringes
10 Single-dose 0.5 mL Syringes
Pneumococcal 15-valent
Conjugate Vaccine
VAXNEUVANCE™
Suspension for intramuscular injection
NDC 0006-4329-03
10 Single-dose 0.5 mL Syringes
REFRIGERATE
Pneumococcal 15-valent
Conjugate Vaccine
VAXNEUVANCE™
Suspension for intramuscular injection
For use in individuals 18 years of age and older
Rx only
Each 0.5 mL dose contains 2.0 mcg each of Streptococcus pneumoniae polysaccharide serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4.0 mcg of polysaccharide serotype 6B, 30 mcg of CRM197 carrier protein, and 125 mcg of aluminum as aluminum phosphate adjuvant.
Contains no preservative.
MERCK
N 3 0006-4329-03 2
Encoding area: Space reserved for 2D Serialization Barcode, Serial Number, Expiry and Lot
10 Single-dose 0.5 mL Syringes
REFRIGERATE
Store in a refrigerator, 2°C to 8°C (36°F to 46°F). DO NOT FREEZE.
Keep container in the outer carton to protect from light.
Fully resuspend by holding horizontally and shaking vigorously prior to use.
See accompanying Prescribing Information for additional details.
Inject intramuscularly.
The tip cap and plunger stopper of the prefilled syringe are not made with natural rubber latex
For product and service information, call 1-800-672-6372.
Manufactured by:
Merck, Sharp & Dohme Corp., a subsidiary of
MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA
U.S. Govt. Lic. No. 0002
At: MSD Ireland (Carlow)
County Carlow, Ireland
Made in Ireland.
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GTIN
SN
EXP
LOT
00300064329032
7008113900

VAXNEUVANCE

pneumococcal 15-valent conjugate vaccine crm197 protein adsorbed injection, suspension

Product Information			
Product Type	VACCINE	**Item Code (Source)**	NDC:0006-4329
Route of Administration	INTRAMUSCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
STREPTOCOCCUS PNEUMONIAE TYPE 1 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 54EC0SE5PZ) (STREPTOCOCCUS PNEUMONIAE TYPE 1 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:54EC0SE5PZ)	STREPTOCOCCUS PNEUMONIAE TYPE 1 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 3 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 2VF3V7175U) (STREPTOCOCCUS PNEUMONIAE TYPE 3 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:2VF3V7175U)	STREPTOCOCCUS PNEUMONIAE TYPE 3 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 4 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: TGJ6YZC4W7) (STREPTOCOCCUS PNEUMONIAE TYPE 4 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:TGJ6YZC4W7)	STREPTOCOCCUS PNEUMONIAE TYPE 4 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 5 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 5SKG37872O) (STREPTOCOCCUS PNEUMONIAE TYPE 5 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:5SKG37872O)	STREPTOCOCCUS PNEUMONIAE TYPE 5 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 6A CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: Z9HK08690W) (STREPTOCOCCUS PNEUMONIAE TYPE 6A CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:Z9HK08690W)	STREPTOCOCCUS PNEUMONIAE TYPE 6A CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 6B CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 4M543JVT7G) (STREPTOCOCCUS PNEUMONIAE TYPE 6B CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:4M543JVT7G)	STREPTOCOCCUS PNEUMONIAE TYPE 6B CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	4 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 7F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 0K0S2P98ZJ) (STREPTOCOCCUS PNEUMONIAE TYPE 7F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:0K0S2P98ZJ)	STREPTOCOCCUS PNEUMONIAE TYPE 7F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 9V CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 5Q768OY0GI) (STREPTOCOCCUS PNEUMONIAE TYPE 9V CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:5Q768OY0GI)	STREPTOCOCCUS PNEUMONIAE TYPE 9V CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 14 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: SK54I0S386) (STREPTOCOCCUS PNEUMONIAE TYPE 14 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:SK54I0S386)	STREPTOCOCCUS PNEUMONIAE TYPE 14 CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 18C CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: XK87D9J012) (STREPTOCOCCUS PNEUMONIAE TYPE 18C CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:XK87D9J012)	STREPTOCOCCUS PNEUMONIAE TYPE 18C CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 19A CAPSULAR	STREPTOCOCCUS	

POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: B970MQT365) (STREPTOCOCCUS PNEUMONIAE TYPE 19A CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:B970MQT365)	PNEUMONIAE TYPE 19A CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 19F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 2E1M7F958B) (STREPTOCOCCUS PNEUMONIAE TYPE 19F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:2E1M7F958B)	STREPTOCOCCUS PNEUMONIAE TYPE 19F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 22F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: U1E9VSB2K2) (STREPTOCOCCUS PNEUMONIAE TYPE 22F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:U1E9VSB2K2)	STREPTOCOCCUS PNEUMONIAE TYPE 22F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 23F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 25N8E57V6T) (STREPTOCOCCUS PNEUMONIAE TYPE 23F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:25N8E57V6T)	STREPTOCOCCUS PNEUMONIAE TYPE 23F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
STREPTOCOCCUS PNEUMONIAE TYPE 33F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN (UNII: 9WP2BC3I04) (STREPTOCOCCUS PNEUMONIAE TYPE 33F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN - UNII:9WP2BC3I04)	STREPTOCOCCUS PNEUMONIAE TYPE 33F CAPSULAR POLYSACCHARIDE DIPHTHERIA CRM197 PROTEIN CONJUGATE ANTIGEN	2 ug in 0.5 mL
CORYNEBACTERIUM DIPHTHERIAE CRM197 PROTEIN (UNII: 08VC9WC084) (CORYNEBACTERIUM DIPHTHERIAE CRM197 PROTEIN - UNII:08VC9WC084)	CORYNEBACTERIUM DIPHTHERIAE CRM197 PROTEIN	30 ug in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
HISTIDINE (UNII: 4QD397987E)	
POLYSORBATE 20 (UNII: 7T1F30V5YH)	
ALUMINUM PHOSPHATE (UNII: F92V3S521O)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0006-4329-03	10 in 1 CARTON		
1	NDC:0006-4329-01	0.5 mL in 1 SYRINGE, GLASS; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		
2	NDC:0006-4329-02	1 in 1 CARTON		
2	NDC:0006-4329-01	0.5 mL in 1 SYRINGE, GLASS; Type 3: Prefilled Biologic Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125741	11/18/2020	

Labeler - Merck Sharp & Dohme Corp. (001317601)

Revised: 8/2021 Merck Sharp & Dohme Corp.